Results: The microtissues presented a core of SSc fibroblast as revealed by vimentin staining and an external layer of keratinocytes as revealed by cytokeratin 10 staining, mimicking the human skin architecture. Gene expression analysis following TGFβ stimulation displayed induced expression of extracellular matrix gene *COL1A1* (p=0.044) and the myofibroblast marker *ACTA2* (p=0.018), indicating that the microtissues were able to develop a fibrotic response. Microtissues, where H19X was silenced, displayed reduced gene expression of *COL1A1* and *ACTA2* after TGFβ stimulation (*COL1A1* p=0.007, *ACTA2* p=0.045). Additionally, H19X silencing led to lower levels of αSMA protein expression (p=0.009) and pro-collagen1α1 secretion (p=0.039) in the supernatant of the microtissue cultures as revealed by Western Blot and ELISA, respectively. *FN1* expression and fibronectin protein levels were not significantly reduced in the microtissues after H19X silencing.

Conclusion: We were able to produce a 3D microtissue resembling skin architecture that can respond to fibrotic stimuli. Knockdown experiments of pro-fibrotic lncRNA H19X confirmed the potential of the model as screening platform for novel pro-fibrotic effectors. A future aim will be to optimize the model for high-throughput automated screening platforms.

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OP0249

SERUM PROTEOMIC BIOMARKERS DEFINE PATIENTS WITH SYSTEMIC SCLEROSIS WITH INTERSTITIAL LUNG DISEASE

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Background: Systemic sclerosis (SSc) is a systemic condition affecting multiple organs and thus being burdened by high morbidity and mortality; disease management is based largely on the early detection of organ involvement, particularly in the case of interstitial lung disease (ILD), ideally through noninvasive biomarkers. Beside serum autoantibodies associated with diffuse SSc, there is currently no reliable serum marker to predict the onset of SSc organ involvement, monitor its progression, and foresee the response to treatments. Proteomic analysis based on aptamer technology is a powerful method with the potential to address this unmet need in SSc.

Objectives: To identify serum biomarkers associated with ILD in SSc.

Methods: Serum samples from 6 women with SSc (3 with ILD at high-resolution pulmonary CT scan) and 7 age-matched female healthy controls (HC) were analyzed using the SOMAscan platform (SomaLogic, Inc., Boulder, CO, USA) to test more than 1300 proteins even at femtomolar concentration. Subsequent validation of candidate proteins was performed using ELISA in an independent cohort of 88 patients with SSc and 48 HC. Statistical analysis included Student's t-test and was assessed using the SomaSuite software (SomaLogic, Boulder, CO, USA).

Results: The proteomic analysis identified 33 proteins with significantly different serum levels in SSc cases compared to HC and 9 proteins differentiating SSc patients according to ILD (Table 1). Compared to HC, SSc sera manifested an altered expression of proteins involved in extracellular matrix formation and cell-cell adhesion (with higher Calpain, EphA5, IDS, MATN2, MMP-12, TNFR4, and lower desmoglein-1, SNP25), angiogenesis (with higher anti-angiogenic factors as angiopoietin-2 and kininogen high molecular weight) lymphocyte recruitment, activation, and signaling (with higher CXCL-1, LAG3 and lower SH21A) with an overall inhibition of neutrophil function (with lower G-CSF-R, CD177, calgranulin B).

Table 1. Significantly altered proteins at serum proteomic analysis of systemic sclerosis (SSc) with or without interstitial lung disease (ILD) and healthy controls (HC)

SSc versus healthy controls		SSc with ILD versus SSc without ILD and healthy controls	
Increased	Reduced	Increased	Reduced
Aldolase A	Adrenomedullin	FCRL3	BAFF
Angiopoietin-2*	ASGR1	IL-22BP**	DERM
C1QR1	C1s	MCP-3	
Calpain	C5	PDE11	
COLEC12 Eotaxin	Calgranulin B	PGP9.5	
EphA5	CD177	sICAM-5	
Fractalkine/CXCL-1	Desmoglein-1	Stratifin	
Granulins	Flt-3 ligand		
IDS Kininogen, HMV	G-CFS-R		
LAG-3	IL-1Ra		
Lamin-B1	Leptin		
LRP1b	Lypd3		
MATN2	SH21A		
MMP-12	SNP25		
STAT1 TMR4	TPBS2		

*significantly increased also at ELISA** significantly increased at ELISA only in SSc with ILD versus HC

The majority of proteins with higher levels in SSc with ILD compared to SSc without ILD were involved in intracellular signaling and cell cycle (FCRL3, PDE11, Stratifin), along with higher MCP-3, a monocyte chemoattractant, and sICAM-5, ligand for the leukocyte adhesion protein LFA-1. Of note, we found that increased IL-22BP, antagonist of IL-22, and decreased BAFF levels characterized SSc with ILD.

Conclusion: Aptamer proteomic analysis allowed to define serum profiles differentiating SSc patients from healthy controls and SSc with ILD from SSc without ILD; the proteins identified are involved in SSc pathogenic pathways and after further investigation on larger cohorts they can be used as reliable biomarkers.

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Imaging in axial spondyloarthritis – what is new?___

OP0250

MRI VERTEBRAL CORNER INFLAMMATION AND FAT DEPOSITION ARE ASSOCIATED WITH WHOLE SPINE LOW DOSE CT DETECTED SYNDESMOPHYTES: A MULTILEVEL ANALYSIS

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Background: A few studies have shown an association between vertebral corner inflammation (VCI) and vertebral corner fat deposition (VCFD) on MRI and syndesmophyte formation on cervical and lumbar conventional radiography.

Objectives: To investigate whether magnetic resonance imaging (MRI) patterns of VCI, VCFD and a combination of both are associated with the development of new or grown syndesmophytes as detected by whole spine low dose computed tomography (ldCT), thereby studying these associations also in the thoracic spine.

Methods: Patients in the Sensitive Imaging in Ankylosing Spondylitis cohort underwent MRI at baseline, 1 year and 2 years, and ldCT at baseline and 2 years. MRI lesions were scored by 3 central readers, using the SPARCC method for VCI and the CanDen method for VCFD, and coded as absent or present per timepoint and per reader. MRI patterns over time (Table) were based on patterns studied by Machado et al.¹ and deemed present if seen by ≥2 out of 3 readers. The patterns reflect hypothetical associations between presence and absence of VCI and VCFD, independently and combined, on ldCT detected new or grown syndesmophytes. Individual reader change scores were used for ldCT images, scored by 2 central readers with the Computed Tomography Syndesmophyte Score. New (CTSS 0 to 1, 2 or 3) and grown (CTSS 1 to 2 or 3; 2 to 3) syndesmophytes were grouped together to represent bone formation. Corners not at risk